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## VEGETABLE MEDICINES OF THE IPECAC CLASS.\*

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THE group of medicines here considered is a very large one, its development having resulted partly from the medical practices of aborigines, and partly from those of educated physicians. Every physician whose practice extends among the lower classes will appreciate the fact that savages are deeply impressed with the importance of emetics and cathartics. To these they assign simple names which indicate such properties,† and in different sections where the same or similar languages are used, different articles come to be designated by the same or similar names. While agreeing in the production of this one effect, these medicines may be as unlike in physiological action and therapeutic application as their plants are in botanical structure. They may but present symptomatic analogies. Upon the introduction of a member of such a group to civilization, if it chance to "take," the others are quickly brought for-

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† As, *ipe-kaa-guena* = a creeping plant which will cause vomiting.

ward. Ipecac was thus introduced during the seventeenth century, and, although proposed as an antidysenteric, its powerful emetic properties made a deep impression upon the medical practitioners of that early period, so that from the very first it occupied a very prominent position, and soon became a sort of a type, around which were grouped not only the other varieties of ipecac which were sought out and brought to Europe, but all drugs possessing properties at all like it. This position ipecac has maintained, as its usefulness and importance have grown almost steadily during two hundred years, and its group has received constant accessions up to the immediate present. So large indeed has it become that several special works in different languages have been devoted to the enumeration and description of its members, the most recent being the *Étude des ipécacuanas*, by Edouard Jacquemet, published in Paris in 1890. As a matter of mere historical interest, it would, perhaps, be not worth while to occupy your time with a consideration of these medicines. It is the practical features of the case to which I wish to direct your attention. Not only is it desirable, in the case of such important agents, to discriminate clearly between their several special fields of application, but it is no small matter to know where and how to search intelligently for a satisfactory substitute in case of emergency. The recent and present scarcity and costliness of ipecac, with its consequent increased tendency toward adulteration and inferiority, almost constitute an emergency, or are liable at any time to do so.\*

My purpose is, therefore, to classify this great group, separating those members which exhibit mere resemblances to ipecac from those which are really like it in physiologi-

\* Since this was penned, accounts of extensive adulteration of ipecac have appeared.

cal action, the only sound basis of therapeutic application. For such comparison I first present an analysis of the properties of ipecac itself.

The action of ipecac lies in two entirely distinct and fully understood directions, besides producing certain other as yet imperfectly understood effects. The first is its local irritation ; the second, its effects, after absorption, upon the vagi. Its imperfectly understood effects are the expectorant, cutaneous, and hepatic.

Its locally irritant effects are very simple and exhibited both externally and internally—externally, in the hyperæmia, pustulations, and even ulcerations produced in direct experiment and in collecting and working with the drug ; internally, in the sneezing and asthmatic seizures dependent upon inhalation, as well as in the nature of its effects upon the digestive mucous membrane. We find that stomach administration produces emesis much more quickly than other modes. That this difference is due to local irritation is shown by the fact that agents which tend to mollify such irritation, like bismuth and hydrocyanic acid, postpone the emesis. Direct observation has shown, moreover, that there is hyperæmia and increased temperature of the intestinal mucous membrane, and often purging, after contact of the ipecac or during its elimination by that tissue.

Its effect upon the vagi is indicated by the occurrence during intense poisoning of symptoms corresponding to those caused by section of the vagi—namely, sudden impeding of the lungs. When death occurs as the result of ipecac poisoning, it is usually in the form of respiratory paralysis. Moreover, if the vagi be first severed, the hypodermic administration of the active constituent of ipecac—emetine—will not produce emesis.

Some of the effects of ipecac, notably vomiting, are ex-

plained by these two properties. The vomiting is doubtless due more especially to the central action of the drug, because it is of slow action, as though the local effects were not sufficient until after the central action had come to their aid. Sometimes repeated doses will fail to produce emesis and the subject will become narcotized.

Cerebral congestion is found to be entirely indirect, due to the strain in vomiting.

The evacuation of bile, both by stomach and bowels, is partly explained by the nature of the vomiting, in which the diaphragm is fixed from above, and the stomach, liver, and gall-bladder are squeezed between it and the abdominal walls. But, in addition to this mechanical evacuation and stimulation, it appears that the liver must be affected in some other way, for the bilious stools are even more pronounced after toleration is established and all tendency to emesis is absent.

We do not understand, or at least are not agreed as to, the expectorant action of ipecac, especially upon the bronchial lining, its diaphoretic action, or its occasional reduction of cutaneous temperature. In its expectorant action it increases the secretion of the parotid glands and of the mucous membranes of the mouth, nose, pharynx, and bronchial tubes. Its action upon the bronchial tubes is especially marked in children, and is powerfully accentuated by combining with it some synergist, the result being greater than would be accounted for by the result of the one plus that of the other. The same may be said of its action upon the skin, and it is important to note that this action is not strong, regular, or certain.

Ipecac exerts no action upon the pulse, blood-pressure, and general temperature, in most cases.

Although not accepted by most physiologists, it would appear as though ipecac must relax the muscles of the

arterioles by peripheral paralysis of the vaso-motor nerves, at least in certain parts.

For therapeutical purposes, and especially in estimating the comparative value of any similar agent, the important points to note are that the effects of ipecac are diverse; that usually only a part of them are desired, the others being often very undesirable, or even intolerable, and that its most useful action is usually the most difficult to secure, except by combining something with it. According as these disadvantages are shared by its associates, their degrees of usefulness and value should be accorded.

With these facts in mind we are prepared to briefly consider the numerous claimants of ipecac-like properties. A great many of these, it must be remembered, have never been investigated. All that we have to guide us in estimating them is their domestic repute, some hints as to composition, and their botanical relationship to plants whose action is well known.

Those which we shall first consider may be regarded as the really ipecac-like group. In their domestic use, and both in their symptoms and mode of action, they are strikingly like ipecac, and almost any of them would make a good substitute. If ipecac were to become lost to the world and we were obliged to study this group for the best article to replace it, it is doubtful if therapeutics would not be a gainer by this disclosure of her riches, and by finding the enforced substitutes superior to the standard which they replaced.

Apomorphine is too well known to call for description. It may better be classed as an alternative than as a substitute for ipecac, for, while in many cases it is inferior, in other cases it is superior. Unlike ipecac, it has no local action.

Among the near botanical relatives of ipecac we find a

number of similar agents. *Randia dumetorum* yields a fruit a portion of the pulp of which seems to act in a manner identical with that drug. But in a pure form—for it must be carefully separated from the remainder of the fruit—it is hardly as accessible as ipecac.

Although ipecac is commonly called a *Cephaelis*, it is doubtful if it should be held separate from the very large genus *psychotria*, many of whose species apparently possess properties similar to those of our own drug, and which, it is fair to assume, contain the same active constituent. Their comparative value would therefore depend upon their percentage of active constituent and their freedom from undesirable constituents and properties. Among them the *Psychotria tomentosa* is prominent, and has been used as an adulterant. The similar adulterant yielded by *Psychotria emetica* is called the violet-striped ipecac. The black-striped ipecac perhaps comes from the same species. The *Psychotria undata* yields a similar drug, and the large-ringed ipecac is yielded by *Uragoga granatanensis*. *Richardia scabra* yields the small-ringed ipecac. But, while all these are so similar to ipecac that they are in reality forms of it, the difficulty is that they are equally inaccessible, being small roots, growing in the same general part of the world, and equally difficult to collect. Still their availability must never be lost sight of.

The violet family also presents a rich field of search for ipecac drugs. The emetic properties of some common violets have long been known and extensively utilized. Their similarity to ipecac is attested by the nature of the active constituent *violin*, so much like emetine as to have long supported the claim that it was an impure form of that alkaloid. This view has now been abandoned, though the precise nature of the body is yet undetermined. Besides the proper violets—*V. tricolor* and *V. odorata*—the ionidi-

ums in this family possess in a marked degree the same properties. The *Ionidium ipecacuanha*, Vent., contains five per cent. of the violin, and is not only ipecac-like in properties, but, because of its close resemblance, it has been used as an adulterant, its root being known as white ipecac. The *Ionidium parviflorum*, *I. itouba*, *I. atropurpureum*, *I. poaya*, and *I. marcutii*, all share more or less the same properties and uses. Should it ever be found necessary, practitioners would doubtless find themselves very well contented to rely upon a plentiful and good stock of ionidium root for at least most of the purposes for which ipecac is now used.

Last of this group we consider the family which apparently takes highest rank among those which we are considering—namely, the *Meliaceæ*, not represented with us except by the *Melia azedarach*, the pride of India or flower of Paris, cultivated in the open air of our Southern States. Some of the members of this family are too violent, like the *Walsura piscidia*, a fish poison of India, described as “a dangerous emmenagogue and violent emetic.” But most of them are mild and efficient. The *Naregamia alata* of India is known commonly as Goanese ipecac, because in the province indicated it is generally used in that way. It has been considerably tried in hospital practice, and the reports say that, as an emetic and expectorant, it has given “results similar to those obtained from ipecacuanha given in equal doses.” Its active principle is a crystallizable alkaloid. Various plants of this family possess names indicative of their properties, as *Trichelia emetica* of Arabia, and *Guarea emetica* and *Guarea purgans* of South America. *Guarea Aubletii* of Colombia is there considered “an excellent substitute for ipecac.” The drug of this family which has been the most thoroughly studied and proved is the bark of one of these guareas, probably undescribed and

commonly known as cocillana. All things considered, it is the most available and desirable of all the ipecac substitutes. As its properties are typical of its relatives in the family and of the class in general, I introduce a condensed sketch of its nature and uses. Professor David D. Stewart, of the Jefferson Medical College, was the first to give it an extended clinical trial, and he concluded that, "as regards the sphere of influence of the two drugs on the respiratory organs, the effects are not unlike those of ipecac, and that it possesses therapeutic properties which render it even superior to ipecac in certain diseases of the air passages in which the latter is often used." These are specified as bronchial catarrh, especially the subacute and chronic forms, when accompanied by scanty or moderately profuse secretion, whether the cough be tight or loose. The cough becomes less frequent and difficult, and the secretion less viscid and more easily expectorated. At the same time loss of appetite is markedly corrected. Some time later Dr. R. W. Wilcox, of the New York Post-graduate Medical School, made an extremely careful series of studies, taking cases as nearly as possible alike, and treating one set with ipecac, another with apomorphine, and a third with cocillana. He concluded that cocillana acts more upon the glands, and is preferable in acute bronchitis in those cases first seen after forty-eight hours. Its effect is long continued, so that doses need not be given at such short intervals. In cases seen earlier he found it best to start expectoration with apomorphine, and keep it up with concillana. In subacute and chronic bronchitis the cocillana was especially serviceable. Its effects are surer than those of either ipecac or apomorphine. It is mildly laxative. It is to be avoided in senile bronchitis. In chronic diseases of pulmonary tissue, cough and expectoration diminish, and night-sweats, inappetence, and constipation are relieved. He says, finally, that it is superior

to ipecac and can with propriety entirely supersede it, and that it is superior to apomorphine, except in the early stages of acute bronchitis. The last investigator to present a complete report upon this drug was Dr. J. W. Eckfeldt, professor of *materia medica* and therapeutics in the Medico-chirurgical College of Philadelphia, who spent two years in systematically studying it before presenting his report. His conclusions are the same as those given above, except that he does not find it counter-indicated in senile bronchitis. He has found it serviceable in pneumonia and hay asthma. He indorses it as one of the finest modern acquisitions to *materia medica*, and believes it superior to ipecac for all the purposes for which that drug is used.

During the recent epidemic of influenza or grip, leading German practitioners claim to have met with excellent results from the cocillana treatment.

The second group to be considered is one in which the resemblance to ipecac is strong—things which might, under stress, be used in place of it, but which no one would claim as approaching it in efficacy or desirability. The most pronounced of this class are from plants with milky juices, though of diverse botanical relationship. Among them are some of the *Euphorbiaceæ*, notably the *E. ipecacuanha* and *E. corollata*. The name of the former is sufficient to indicate its supposed relation to ipecac. But while they determine emesis, expectoration, and diaphoresis, they show their relation to castor oil by combining a strongly cathartic tendency. If given in small doses their ipecac action is by no means certain, while if we increase it we get a very indefinite amount of purging; in some cases uncontrollable and dangerous. After long and persistent trial their use has been mostly abandoned. The natural order *Asclepiadaceæ* furnishes a number of milky-juiced plants which belong in this group, of which the officinal *asclepias*

or pleurisy-root may be taken as the type medicinally. Its use is not admissible as an emetic, but it is both expectorant and diaphoretic. It seems strange that authors do not agree as to the mode of action of so old, important, and much-used a drug, but by some—and probably correctly—it is put into the stimulant or irritant class, while by others this view is disputed. Certainly it reduces the heart's action and the blood-pressure. If given to the point of emesis it is also liable to purge. The ancient and celebrated madar or mudar, of Asia and Africa, is a root bark from *Calatropis procera* and *C. gigantea*, related to our asclepias. These have been freely urged in substitute for ipecac, but their active constituent seems to be very dissimilar and they act entirely through local irritation. The original use of this, like ipecac, as an antidyseenteric, unfortunately sheds little light upon its properties, because of the very indefinite application of the term "dysentery." Both the roots and leaves of the related plant *Tylophora asthmatica*, of India, have been urged in exactly the same way. Except in its tendency to purge, clinical reports show a marked similarity of this drug to ipecac. *Tylophora fasciculata*, *Dæmia extensa*, and *Dregia volubilis*, all fall more or less clearly into this group. Most of you have probably seen our little plant *Asarum canadense*, or Canada snake-root, which has been so strongly urged for introduction to the pharmacopœia. As its common name indicates, it is an aromatic stimulant. It seems a little strange that the very similar *Asarum europæum* should have been lauded as an ipecac drug, and largely used as its substitute in some parts of Europe. I have not been able to find any information concerning its physiological action to support this view. *Gillenia* yields two species of beautiful North American plants, somewhat related to the strawberry and blackberry, but emetico-cathartic rather than astringent like those

plants. The external resemblance of the root of *Gillenia trifoliata* to ipecac has caused it to be used as an adulterant, and, strangely enough, its properties also have been found similar. But it is much less effective, and its common name of Indian physic indicates an important difference in action. There is no doubt, however, that this would serve as a fair substitute in the absence of anything better.

The third group we may call the *tobacco group*. Should one attempt to use tobacco to secure emesis he would find almost the maximum of distress accompanying the minimum of emesis, whereas he should seek exactly the opposite combination. Great nausea and extreme depression would precede the vomiting. If he used it as an expectorant, he would find that while it increased the supply of mucus there would be no stimulus to carry this away. On the contrary, it acts strongly toward paralysis of the respiratory apparatus. Its perspiration is a cold one, accompanying an unhealthy condition of the skin. Lobelia is a drug of the same general type, though much less objectionable. Although its expectorant action can be secured without an extreme degree of disorder, it weakens both the circulation and respiration preceding its emetic action. In tropical America we find a considerable number of related plants, some *Lobelias*, some *Tupas*, and some in the genus *Siphocampylos*, which the natives use to produce tobacco-like or lobelia-like effects, on account of which they have been compared to ipecac. The natural order *Acanthaceæ* yields various plants, as *Adhatoda*, *Ruellia*, and *Gendarussa*, whose physiological action has not been well established, but which apparently belong to the tobacco group. The same may be said of some bignoniacs.

Group 4 are essentially nervines. Their action upon the nervous system may be immediate or it may be through cir-

culatory disarrangements, but in some way the prominent effect is a great modification of the nervous functions. The distinctively cardiant division of this group contains the three *Veratrum*s—*viride*, *album*, and *nigrum*—cevadilla, scilla, *Crinum toxicarium*, and some other related monocotyledonous plants. The powerful depresso-motor effects of these plants are well typified by the almost uncontrollable vomiting of *Veratrum viride*. The vomiting depends clearly upon derangements of the cerebral circulation. Various species of narcissus would appear at first thought to pertain to this group, but there is evidence to show that the resemblance of their action to that of ipecac may be much more real. Very similar in action to these monocotyledons are a number of poisonous *Leguminosa*—namely, laburnum, baptisia, sophora of various species, *Clitoria ternatea*, broom, etc. Plants whose action is not well determined, but which appear to belong here, are *Datisca cannabina*, *Atriplex hortensis*, and several species of Boerhaavia.

The "harsh" emetics may stand as our fifth group. In kind they are very similar to group 6, but differ so greatly in degree as to introduce a different feature into the effects—namely, the possible production of so great an irritation or inflammation as to cause prostration or collapse. That is, they are irritant poisons and pseudo-narcotics. It will at once occur to you that these characters will admit a large number of drugs, for so many of our powerful medicines are capable of producing this form of emesis. But I am here restricting myself to those things in which the effects for which ipecac is used are so conspicuous among the other properties, that the articles have been proposed as substitutes for that agent. Even thus the group is large enough and varied enough to be properly subdivided. Some of the members, in moderate doses, effect no conspicuous action upon the bowels sufficient to stamp them as cathartics. To

this subdivision may be referred the powerful irritant meze-reum, some plants of the buttercup family, perhaps the *Wückstræmia Forsteri* of Tahiti (related to the tea plant), and some irritant poisons of the natural order *Menispermaceæ*. In the other subdivision the primary tendency is toward catharsis, the emesis postponed until after catharsis has failed to be excited or to relieve. This group includes the drastics, gamboge, podophyllum, elaterium, bryony and melon-root, *Cyclamen europæum*, and others of the primrose family (not the evening primrose family or *Onagrarieæ*), and perhaps *Calophyllum inophyllum* and the gratiolas. The *Vandellia diffusa* seems to be in some respects like these, in others like the tobacco group. Croton oil, curcas seeds, *Hura crepitans*, etc., of the natural order *Euphorbiaceæ*, appear to belong here, while others of this large family must be ranked, as previously stated, much nearer the ipecac in properties and mode of action. Attention is called to the fact that none of these harsh emetics are true nervines. As I have said, they may be pseudo-narcotics, but the nervous effects are reflex and secondary, resulting from the severe irritation. *Iris versicolor* and colchicum might be placed here, though they would require special characterization, especially colchicum. The profound disturbances which are a prerequisite for emesis by these plants render them all not commendable as ipecac substitutes.

Group 6 are also irritant emetics, though they can not properly be called harsh. They are those of the mustard type, act only when introduced by the stomach, and then not through absorption. They are, like the next group, more efficient when administered in bulky form, but differ from that group in their specific irritant properties. The term "reflex emetics" has been applied to them, as well as to the last. Besides the mustards, the group includes various plants of the *Capparideæ*, the family yielding our capers,

and the *Stanleya pinnatifida*, which vomited a party of early explorers under the botanist Nuttall, they having eaten it for its large cabbage-like leaves.

Another group, more distinctly irritant than these, yet not so irritant as the harsh emetics, may be laxative, but this property is slight and incidental. They act as emetics through their direct effect upon the gastric nerves. Their stimulant-expectorant powers are marked. The best known of them contain saponin in considerable quantity. Here we place senega, saponaria, quillaia or soap-bark, sarsaparilla, (in part), and the horse-chestnut. Besides our official *Polygala senega*, a large number of species of polygala are used in various parts of the world in the same way. Most notable is the *P. poaya*, of Brazil.

The last group to be considered is the most distant of all from the true ipecac. It is well illustrated by the *Eupatorium perfoliatum*, the old-fashioned boneset or thoroughwort, which, taken in the form of extract or fluid extract, produces none of its sudorific or expectorant effects, except slightly, through general stimulus, and gives no hint toward emesis. These results come from administering it in large quantities of water, whereas a minute portion of the active principle of ipecac—emetine—given hypodermically, is efficient.

With boneset go all the many species of eupatorium used here and in other countries, the related senecios, elder flowers, linden flowers, and most of the old-fashioned herbs used in the same manner and for the same purpose. Here also probably belongs the *Ilex vomitoria*, or Southern holly, yielding the black drink of the Southern aborigines, concerning which plant a book has recently been written. Other species of ilex fall within the same group. This group is represented in the practice of almost all uncivilized classes.

We must conclude from this study that ipecac, even when strictly considered, is not a unique remedy; that while the very great majority of drugs which have been associated with it are not really of the same type, a number of them are and could, in emergency, yield products equally satisfactory; and that one of them at least is already proved to be capable of immediately superseding it with advantage.

